REMARKS

Two claims (1703 and 1784) have been amended and one claim (1796) has been canceled in the claim listing above.

After entry of the claims identified in the complete listing above, the status of the claims will be as follows:

Amended claims: 1703 and 1784.

Canceled claims: 1796.

New claims added: None

Pending claims presented for further examination: 569-571, 573-575, 577, 582-589, 592-594, 597-600, 602-604, 607-608, 610-612, 614-624, 634-635, 637-638, 641-642, 646, 648-651, 656-661, 667, 670, 707-714, 716-717, 719-723, 725-727, 729, 734-747, 749-752, 754-756, 759-760, 762-764, 766-776, 786-787, 789-790, 793-794, 796-797, 800-803, 808-813, 819, 822, 859-866, 868-869, 871-875, 877-879, 881, 886-899, 901-904, 906-908, 911-912, 914-916, 918-928, 938-939, 941-942, 945-949, 952-955, 960-965, 971, 974, 1011-1018, 1020-1021, 1023-1027, 1029-1031, 1033, 1038-1051, 1053-1056, 1058-1060, 1063-1064, 1066-1068, 1070-1080, 1090-1091, 1093-1094, 1097-1099, 1101, 1104-1107, 1112-1117, 1123, 1126, 1163-1170, 1172-1173, 1175-1179, 1181-1183, 1185, 1190-1200, 1204, 1208-1209, 1212-1216, 1218-1244, 1248-1249, 1253, 1255-1258, 1263-1270, 1272, 1275, 1278-1294, 1296-1328, 1331-1332, 1334-1351, 1353-1354, 1357-1358, 1360, 1362-1369, 1372-1380, 1383, 1386-1391, 1393-1407, 1409-1487, 1490-1491, 1493-1499, 1504-1516, 1518, 1520-1525, 1527, 1530-1539, 1541, 1544-1568, 1570-1585, 1587, 1592-1612, 1614-1615, 1618-1621, 1623-1628, 1631-1632, 1635-1647, 1649-1656, 1658, 1660-1667, 1670-1677, 1679-1680, 1682, 1685-1722, 1727-1739, 1742-1757, 1760-1768 and 1776-1795.

This paper follows a telephone call on November 4, 2005 between Primary Examiner John S. Brusca, Group Art Unit 1631, and Applicants' undersigned attorney. During the November 4th call, Examiner Brusca requested clarification on the following matters:

(1). Applicants' claim for priority;

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(2). the latest abstract submitted of record;

(3). a minor amendment to Claim 1703; and

(4). written description support for the "nuclease treatment" step recited in Claim 1784.

In response to the call, Applicants are providing (1) the priority information in the form of a new section (Cross-Reference To Other Related Applications). This new section has been added by amendment to page 1 in the specification. This priority information is the same priority information that was provided in Applicants' May 23, 2000 Amendment Under 37 C.F.R. §1.115. A copy of page 3 from their May 23, 2000 Amendment is provided as Exhibit A to this paper.

Applicants are also providing (2) a new Abstract Of The Disclosure to replace the prior abstract submitted with their December 31, 2003 Amendment. This new Abstract (Exhibit B) is believed to conform with the requirements of 37 C.F.R. §1.72 and MPEP §608.01b). This new Abstract will enable readers to determine quickly from a cursory inspection the nature and gist of the technical disclosure, as set forth in 37 C.F.R. §1.72. This Abstract also represents a more adequate and clearer statement of the contents of the disclosure, as set forth in MPEP §608.01b).

For Item No. (3), Applicants have amended Claim 1703 in the claim listing above. As the Examiner correctly observed, the recitation of "said metal or metal ion" in line 9 did not find antecedent support in the claim. Accordingly, the word "said" has been changed to -- a --.

For Item No. (4), Applicants would offer the following remarks. The subject matter of Claim 1784 is generally disclosed on page 89 (middle paragraph) in the specification:

> Another aspect of the practices of this invention which is particularly advantageous is to carry out the detection or hybridization in the liquid phase between the DNA sought to be detected and the DNA detecting probe. In this liquid phase system, both the DNA molecule to be detected and the appropriate DNA detecting probe are not attached to any insoluble substrate or any insoluble chemical moiety. The advantages of the liquid phase detection system reside in the speed of hybridization or hybrid formation between the DNA to be detected and the appropriate DNA probe therefor. For example, in a solid-liquid system the time required to effect recognition and hybridization formation is about ten times greater than if it were carried out in a completely liquid system, i.e. both DNA to be detected and the detecting DNA are not attached to an insoluble moiety.

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With respect to the "nuclease treatment" step in Claim 1784, the specification provides in the next page (p. 90, middle paragraph) the following:

> In accordance with the practices of this invention, the identification or characterization of the isolated particles, viruses and bacteria, would be hybridization of the characterizing or identifying DNA thereof with a specific single stranded DNA probe prepared in accordance with the practices of this invention. **After hybridization, excess non-hybridized probe DNA would be digested with S_1 nuclease and exonuclease I** from E. coli at high salt content to suppress the nicking activity of the S_1 nuclease, see Vogt, Methods in Enzymology, Vol. 65, pages 248-255 (1980). **This nuclease treatment would produce mononucleotides from the excess, non-hybridized single-stranded DNA probe but would leave the double-stranded, hybridized DNA intact.** This would then be absorbed at high salt content on Dowex anion exchanger (the nucleotides and the small amount of oligonucleotides will not bind to the resin in high salt concentration). The resulting hybridized DNA would then be identified or characterized by various procedures applicable to the practices of this invention. [emphasis added]

The above paragraph, including the highlighted portions, is believed to support the "nuclease treatment" step recited in Claim 1784.

To clarify the "nuclease treatment" further, however, Applicants have amended Claim 1784 above. Thus, as amended, the step at hand calls for "subjecting said liquid phase to nuclease treatment to digest non-hybridized single-stranded detectable non-radioactively labeled oligonucleotides or polynucleotides and leave said hybrids intact." The foregoing language is believed to comport with the disclosure found on page 90, middle paragraph, in the specification, and just quoted above.

In reviewing the pending claims, Applicants' attorney noticed that Claim 1796 is still pending and was not canceled in their September 19, 2005 Supplemental Amendment. This oversight may have arisen partly out of the September 8, 2005 Advisory Action which was quoted in footnote 1 in their Supplemental Amendment ("The request for interference remains in abeyance as the above issue [new matter rejection of claims 1723-1724, 1740-1741, 1769-1773 and 1775] still

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prevents proceeding with interference proceedings.").[2] Although Applicants continue to believe that their disclosure provides written description support for the use of different fluorescent labeled fragments in nucleic acid sequencing, just as it does for chromosomal karyotyping and genetic disorder detection, they have nevertheless canceled Claim 1796 above. The cancellation of Claim 1796 is done, again, without prejudice or disclaimer to Applicants' rights, and again, to allow for Applicants' September 28, 2004 Request For Interference Pursuant To 37 C.F.R. §41.202 to go forward.

Entry of the above claim amendments and claim cancellation is respectfully requested.

Finally, Applicants would like to bring to the Examiner's attention U.S. Patent No. 6,200,748 B1, issued on March 13, 2001. The '748 Patent issued to California Institute of Technology in the name of Lloyd M. Smith et al. as inventors, and it is based upon the same priority document as U.S. Patent No. 5,821,058, which is referenced in Applicants' September 28, 2004 Interference Request. U.S. Patent No. 6,200,748 B1 came to their undersigned attorney's own attention this past week.

In particular, claims 17-19 of the '748 Patent should be of interest when read against claim 25 of the '058 Patent.

Claims 17-19 read as follows:

> 17. A chain termination DNA sequencing method comprising extending the primer of the duplex of claim 1 by a polymerase to produce a labeled polynucleotide, and separating the labeled polynucleotide from the template.[3]
>
> 18. A chain termination DNA sequencing method comprising extending the primers of the set of duplexes of claim 4 by a polymerase to produce a set of labeled polynucleotides.[4]

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[2] The bracketed parenthetical language was taken from page 3, line 2, in the September 8, 2005 Advisory Action ("The rejection of claims 1723, 1724, 1740, 1741, 1769-1773, and 1775 based on NEW MATTER . . .").

[3] Claim 1 in the '748 Patent recites:

> **1. A duplex comprising an oligonucleotide primer and a template, wherein the primer is covalently coupled to a chromophore or flurophore so as to allow chain extension by a polymerase.**

[4] Claim 4 in the '748 Patent recites:

19. The chain termination DNA sequencing method of claim 18, wherein the set of duplexes comprises four DNA sequencing reactions, wherein each labeled polynucleotide is distinguishable by spectral characteristics of the chromophore or fluorophore covalently coupled thereto.

Claim 25 of the '058 Patent recites:

25. The method according to claim 14, wherein the polynucleotide sequencing technique comprises a Maxam/Gilbert chemical degradation reaction or a Sanger chain-termination reaction.[5]

Before closing on the subject of U.S. Patent No. 6,200,748 B1, it appears that this patent is also the subject of Reissue Application No. 10/389,663, filed on March 13, 2003. The three above-quoted chain termination DNA sequencing method claims from the '748 Patent (17-19) continue to be present in different forms in Reissue Application No. 10/389,663, now as claims 152-154, according to a paper titled "Amendment And Response To Office Action" and dated May 6, 2005. The text of claims 152-154 is set forth below:

152. (New) A chain termination DNA sequencing method comprising extending the synthetic oligonucleotide of the duplex of claim 136 by a polymerase to produce a labeled polynucleotide, and separating the labeled polynucleotide from the template.[6]

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4. A set of duplexes comprising two or more of the duplexes of claim 1.

[5] **Claim 14 in the '058 Patent recites:**

14. A method of determining the sequence of a polynucleotide by analyzing polynucleotide fragments generated by a polynucleotide sequencing technique, each of said polynucleotide fragments being tagged with a chromophore or fluorophore, comprising:

introducing the tagged polynucleotide fragments into an electrophoretic medium;

separating the tagged polynucleotide fragments in said electrophoretic medium using an electrophoretic procedure capable of resolving said polynucleotide fragments differing in length by a single nucleotide;

detecting the separated tagged polynucleotide fragments by means of the chromophore or flurophore; and

determining the polynucleotide sequence from the polynucleotide fragments detected.

[6] **Claim 136 in Reissue Application No. 10/389,663 recites:**

153. (New) A chain termination DNA sequencing method comprising extending the synthetic oligonucleotides of the set of duplexes of claim 139 by a polymerase to produce a set of labeled polynucleotides.[7]

154. (New) The chain termination DNA sequencing method of claim 153, wherein the set of duplexes comprises four DNA sequencing reactions, wherein each labeled polynucleotide is distinguishable by spectral characteristics of the fluorophore covalently attached thereto.

The last paper in Reissue Application No. 10/389,663 appears to be a final Office Action mailed on July 5, 2005 by Primary Examiner Jeffrey Friedman, Group Art Unit 1637.

It is respectfully requested that consideration be given to U.S. Patent No. 6,200,748 B1 and Reissue Application No. 10/389,663, particularly as any of these documents and proceedings may relate to Applicants' September 28, 2004 Interference Request and their present application.

Favorable action is also respectfully requested.

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136. (New) A duplex comprising a synthetic oligonucleotide and a template, wherein the synthetic oligonucleotide is from 9 to 50 bases in length, and wherein the synthetic oligonucleotide is covalently coupled to a fluorophore so as to allow chain extension by a polymerase.

[7] Claim 139 in Reissue Application No. 10/389,663 recites:

139. (New) A set of duplexes comprising two or more of the duplexes of claim 136.

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SUMMARY AND CONCLUSIONS

Two claims (1703 and 1784) have been amended and one claim (1796) has been canceled in the claim listing above.

In view of the single claim cancellation, no additional claim fees are due in connection with this paper. In the event that any additional fees are due, however, Applicants hereby request that the Patent and Trademark Office charge the amount of any such fees to Deposit Account No. 05-1135, or to credit any overpayment thereto.[8]

If a telephone conversation would further prosecution of the application, the Examiner is invited to call Applicants' undersigned attorney at the number below.

Early and favorable action is respectfully requested.

Respectfully submitted,

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[8] **As indicated above on the first page, this paper is accompanied by a Request For Extension Of Time (Additional Two Months), and authorization for the fee therefor.**

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